

SEQUENCE LISTING

<110> Umana, Pablo  
Bruenker, Peter  
Ferrara, Claudia  
Suter, Tobias

<120> Fusion Constructs and Use of Same to Produce Antibodies with  
Increased Fc Receptor Binding Affinity and Effector Function

<130> 1975.0180003

<150> US 60/441,307  
<151> 2003-01-22

<150> US 60/491,254  
<151> 2003-07-31

<150> US 60/495,142  
<151> 2003-08-15

<160> 20

<170> PatentIn version 3.2

<210> 1  
<211> 11  
<212> PRT  
<213> Unknown

<220>  
<223> c-myc epitope tag

<400> 1

Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu  
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gcgtgtgcct gtgacccccg cgcccctgct ccagccactg tcccc  
45

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<223> GAB-178 PCR primer

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gaaggtttct ccagcatcct ggtacc  
26

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ctgaggcgcg ccgccaccat gctgaagaag cagtctgcag ggc 43

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ggggacagtg gctggagcag gggcgcgggg gtcacaggca cacgcggc 48

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gctaggccgg ccgccaccat gaagttaagc cgccagttca ccgtgttcgg 50

<210> 7  
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<220>  
<223> GAB-253 PCR primer

<400> 7  
ggggacagtg gctggagcag gggtgagcca gcaccttggc tgaaattgct ttgtgaactt 60  
ttcgg 65

<210> 8  
<211> 66  
<212> DNA  
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<223> GAB-254 PCR primer

<400> 8  
tccgaaaagt tcacaaagca atttcagcca aggtgctggc tcaccctgc tccagccact 60  
gtcccc 66

<210> 9  
<211> 29  
<212> DNA  
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<223> GAB-255 PCR primer

<400> 9  
atgccgcata ggccctccgag caggacccc

29

<210> 10  
<211> 43  
<212> DNA  
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<223> GAB-261 PCR primer

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gctaaatatt gaattccctt tatgtgtaac tcttggtga agc

43

<210> 11  
<211> 48  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> GAB-262 PCR primer

<400> 11  
tagcaatatt gaattcgcag gaaaaggaca agcagcgaaa attcacgc

48

<210> 12  
<211> 1715  
<212> DNA  
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<223> Nucleotide sequence of GnTI-GnTIII

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atgaagttaa gccgccagtt caccgtgttc gccagtgcca tcttctgtgt ggtgattttc 60  
tcgctctacc tgatgctgga ccgggggtcac ttagactacc ccaggaaccc gcgccgcgag 120  
ggctccttcc ctcagggcca gctctcaatg ttgcaagaaa aaatagacca tttggagcgt 180  
ttgctagctg agaataatga gatcatctca aatattagag actcagtcac caatttgagt 240  
gagtctgtgg aggatgggtcc gaaaagttca caaagcaatt tcagccaagg tgctggctca 300  
cccctgctcc agccactgtc ccctagcaag gccaccgaag aactgcaccg ggtggacttc 360  
gtgttgccgg aggacaccac agagtatttt gtgcgcacca aagctggcgg tgtgtgcttc 420  
aaaccaggta ccaggatgct ggagaaacct tctccagggc ggacagagga gaagaccaag 480

gtggctgagg ggtcctcggg cgggggtcct gctcggaggc ctatgcggca tgtgttgagt 540  
gcacgggagc gcctgggagg cgggggcact aggcgcaagt gggttgagtg tgtgtgcctg 600  
ccaggctggc acgggcccag ctgcgggggtg cccactgtgg tccagtattc caacctgccc 660  
accaaggagc gcctggtacc caggaggtg ccgaggcggg ttatcaacgc catcaacatc 720  
aaccatgagt tcgacctgct ggatgtgcgc ttccatgagc tgggcgatgt tgtggacgcc 780  
tttgtggtct gcgaatccaa ttccaccgcc tacggggagc ctcggccgct caagttccga 840  
gagatgctga ccaatggcac ctccgagtac atccgccaca aggtgctcta cgtcttcctg 900  
gaccacttcc cacctggtgg ccgtcaggac ggctggattg cagacgacta cctgcgtacc 960  
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cccagaatgg tgacttcccc cgctgggggtg actacgagga caagagggac ctcaattaca 1440  
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cggaacagaa actgatctct gaagaggacc tntag 1715

<210> 13  
<211> 571  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Amino acid sequence of GnTI-GnTIII

<400> 13

Met Lys Leu Ser Arg Gln Phe Thr Val Phe Gly Ser Ala Ile Phe Cys  
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Val Val Ile Phe Ser Leu Tyr Leu Met Leu Asp Arg Gly His Leu Asp  
20 25 30

Tyr Pro Arg Asn Pro Arg Arg Glu Gly Ser Phe Pro Gln Gly Gln Leu

35	40	45
Ser Met Leu Gln Glu Lys Ile Asp His Leu Glu Arg Leu Leu Ala Glu		
50	55	60
Asn Asn Glu Ile Ile Ser Asn Ile Arg Asp Ser Val Ile Asn Leu Ser		
65	70	75 80
Glu Ser Val Glu Asp Gly Pro Lys Ser Ser Gln Ser Asn Phe Ser Gln		
	85	90 95
Gly Ala Gly Ser Pro Leu Leu Gln Pro Leu Ser Pro Ser Lys Ala Thr		
	100	105 110
Glu Glu Leu His Arg Val Asp Phe Val Leu Pro Glu Asp Thr Thr Glu		
	115	120 125
Tyr Phe Val Arg Thr Lys Ala Gly Gly Val Cys Phe Lys Pro Gly Thr		
	130	135 140
Arg Met Leu Glu Lys Pro Ser Pro Gly Arg Thr Glu Glu Lys Thr Lys		
145	150	155 160
Val Ala Glu Gly Ser Ser Val Arg Gly Pro Ala Arg Arg Pro Met Arg		
	165	170 175
His Val Leu Ser Ala Arg Glu Arg Leu Gly Gly Arg Gly Thr Arg Arg		
	180	185 190
Lys Trp Val Glu Cys Val Cys Leu Pro Gly Trp His Gly Pro Ser Cys		
	195	200 205
Gly Val Pro Thr Val Val Gln Tyr Ser Asn Leu Pro Thr Lys Glu Arg		
	210	215 220
Leu Val Pro Arg Glu Val Pro Arg Arg Val Ile Asn Ala Ile Asn Ile		
225	230	235 240
Asn His Glu Phe Asp Leu Leu Asp Val Arg Phe His Glu Leu Gly Asp		
	245	250 255
Val Val Asp Ala Phe Val Val Cys Glu Ser Asn Phe Thr Ala Tyr Gly		
	260	265 270
Glu Pro Arg Pro Leu Lys Phe Arg Glu Met Leu Thr Asn Gly Thr Phe		
	275	280 285

Glu Tyr Ile Arg His Lys Val Leu Tyr Val Phe Leu Asp His Phe Pro  
 290 295 300  
 Pro Gly Gly Arg Gln Asp Gly Trp Ile Ala Asp Asp Tyr Leu Arg Thr  
 305 310 315 320  
 Phe Leu Thr Gln Asp Gly Val Ser Arg Leu Arg Asn Leu Arg Pro Asp  
 325 330 335  
 Asp Val Phe Ile Ile Asp Asp Ala Asp Glu Ile Pro Ala Arg Asp Gly  
 340 345 350  
 Val Leu Phe Leu Lys Leu Tyr Asp Gly Trp Thr Glu Pro Phe Ala Phe  
 355 360 365  
 His Met Arg Lys Ser Leu Tyr Gly Phe Phe Trp Lys Gln Pro Gly Thr  
 370 375 380  
 Leu Glu Val Val Ser Gly Cys Thr Ile Asp Met Leu Gln Ala Val Tyr  
 385 390 395 400  
 Gly Leu Asp Gly Ile Arg Leu Arg Arg Arg Gln Tyr Tyr Thr Met Pro  
 405 410 415  
 Asn Phe Arg Gln Tyr Glu Asn Arg Thr Gly His Ile Leu Val Gln Trp  
 420 425 430  
 Ser Leu Gly Ser Pro Leu His Phe Ala Gly Trp His Cys Ser Trp Cys  
 435 440 445  
 Phe Thr Pro Glu Gly Ile Tyr Phe Lys Leu Val Ser Ala Gln Asn Gly  
 450 455 460  
 Asp Phe Pro Arg Trp Gly Asp Tyr Glu Asp Lys Arg Asp Leu Asn Tyr  
 465 470 475 480  
 Ile Arg Ser Leu Ile Arg Thr Gly Gly Trp Phe Asp Gly Thr Gln Gln  
 485 490 495  
 Glu Tyr Pro Pro Ala Asp Pro Ser Glu His Met Tyr Ala Pro Lys Tyr  
 500 505 510  
 Leu Leu Lys Asn Tyr Asp Gln Phe Arg Tyr Leu Leu Glu Asn Pro Tyr  
 515 520 525  
 Arg Glu Pro Lys Ser Thr Val Glu Gly Gly Arg Arg Asn Gln Gly Ser  
 530 535 540

Asp Gly Arg Ser Ser Ala Val Arg Gly Lys Leu Asp Thr Thr Glu Gly  
545 550 555 560

Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu  
565 570

<210> 14  
<211> 1722  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Nucleotide sequence of ManII-GnTIII

<400> 14  
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aatgccttgc tgctcctctt cttctggacg cgcccagcac ctggcaggcc accctcagtc 120  
agcgctctcg atggcgaccc cgccagcctc acccggaag tgattcgcct ggcccaagac 180  
gccgaggtgg agctggagcg gcagcgtggg ctgctgcagc agatcgggga tgccctgtcg 240  
agccagcggg ggaggggtgcc caccgcggcc cctcccgcgc agccgcgtgt gcctgtgacc 300  
cccgcgcccc tgctccagcc actgtcccct agcaaggcca ccgaagaact gcaccgggtg 360  
gacttcgtgt tgccggagga caccacagag tattttgtgc gcaccaaagc tggcggtgtg 420  
tgcttcaaac caggtaccag gatgctggag aaaccttctc cagggcggac agaggagaag 480  
accaaggtgg ctgaggggtc ctcggtccgg ggtcctgctc ggaggcctat gcggcatgtg 540  
ttgagtgcac gggagcgcct gggaggccgg ggcactaggc gcaagtgggt tgagtgtgtg 600  
tgccctgccag gctggcacgg gccagctgc ggggtgccca ctgtggtcca gtattccaac 660  
ctgcccacca aggagcgcct ggtacccagg gaggtgccga ggcgggttat caacgccatc 720  
aacatcaacc atgagttcga cctgctggat gtgcgcttcc atgagctggg cgatgttgtg 780  
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ttcctggacc acttcccacc tgggtggcgt caggacggct ggattgcaga cgactacctg 960  
cgtaccttcc tcacccagga tgggtgtctcc cgcctgcgca acctgcgacc tgatgacgtc 1020  
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tggaagcaac caggcacact ggaggtgggtg tcaggctgca ccattgacat gctgcaggct 1200  
gtgtatgggc tggacggcat ccgcctgcgc cgccgtcagt actacaccat gcccaacttt 1260  
cgacagtatg agaaccgcac cggccacatc ctagtgcagt ggtctctcgg cagccccctg 1320

cacttcgcg gctggcactg ctcttggtgc ttcacacccg agggcatcta cttcaaactc 1380  
gtgtcggccc agaatggtga cttcccccg tggggtgact acgaggacaa gagggacctc 1440  
aattacatcc gaagcttgat tcgcactggg ggatgggtcg acggcacgca gcaggagtac 1500  
cctcctgcag accccagtga acacatgtat gtccttaagt acctgctcaa gaactatgac 1560  
cagttccgct acttgctcga aaatccctac cgggagccca agagcactgt agagggtggg 1620  
cgccggaacc agggctcaga cggaaggtca tctgctgtca ggggcaagtt ggatacaacg 1680  
gagggcccg aacagaaact gatctctgaa gaggacctgt ag 1722

<210> 15  
<211> 573  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Amino acid sequence of ManII-GnTIII fusion  
<400> 15

Met Leu Lys Lys Gln Ser Ala Gly Leu Val Leu Trp Gly Ala Ile Leu  
1 5 10 15

Phe Val Ala Trp Asn Ala Leu Leu Leu Leu Phe Phe Trp Thr Arg Pro  
20 25 30

Ala Pro Gly Arg Pro Pro Ser Val Ser Ala Leu Asp Gly Asp Pro Ala  
35 40 45

Ser Leu Thr Arg Glu Val Ile Arg Leu Ala Gln Asp Ala Glu Val Glu  
50 55 60

Leu Glu Arg Gln Arg Gly Leu Leu Gln Gln Ile Gly Asp Ala Leu Ser  
65 70 75 80

Ser Gln Arg Gly Arg Val Pro Thr Ala Ala Pro Pro Ala Gln Pro Arg  
85 90 95

Val Pro Val Thr Pro Ala Pro Leu Leu Gln Pro Leu Ser Pro Ser Lys  
100 105 110

Ala Thr Glu Glu Leu His Arg Val Asp Phe Val Leu Pro Glu Asp Thr  
115 120 125

Thr Glu Tyr Phe Val Arg Thr Lys Ala Gly Gly Val Cys Phe Lys Pro  
130 135 140

Gly Thr Arg Met Leu Glu Lys Pro Ser Pro Gly Arg Thr Glu Glu Lys



145		150		155		160									
Thr	Lys	Val	Ala	Glu	Gly	Ser	Ser	Val	Arg	Gly	Pro	Ala	Arg	Arg	Pro
				165					170					175	
Met	Arg	His	Val	Leu	Ser	Ala	Arg	Glu	Arg	Leu	Gly	Gly	Arg	Gly	Thr
			180					185					190		
Arg	Arg	Lys	Trp	Val	Glu	Cys	Val	Cys	Leu	Pro	Gly	Trp	His	Gly	Pro
		195					200					205			
Ser	Cys	Gly	Val	Pro	Thr	Val	Val	Gln	Tyr	Ser	Asn	Leu	Pro	Thr	Lys
	210					215					220				
Glu	Arg	Leu	Val	Pro	Arg	Glu	Val	Pro	Arg	Arg	Val	Ile	Asn	Ala	Ile
225					230					235					240
Asn	Ile	Asn	His	Glu	Phe	Asp	Leu	Leu	Asp	Val	Arg	Phe	His	Glu	Leu
				245					250					255	
Gly	Asp	Val	Val	Asp	Ala	Phe	Val	Val	Cys	Glu	Ser	Asn	Phe	Thr	Ala
			260					265					270		
Tyr	Gly	Glu	Pro	Arg	Pro	Leu	Lys	Phe	Arg	Glu	Met	Leu	Thr	Asn	Gly
		275					280					285			
Thr	Phe	Glu	Tyr	Ile	Arg	His	Lys	Val	Leu	Tyr	Val	Phe	Leu	Asp	His
	290					295					300				
Phe	Pro	Pro	Gly	Gly	Arg	Gln	Asp	Gly	Trp	Ile	Ala	Asp	Asp	Tyr	Leu
305					310					315					320
Arg	Thr	Phe	Leu	Thr	Gln	Asp	Gly	Val	Ser	Arg	Leu	Arg	Asn	Leu	Arg
				325					330					335	
Pro	Asp	Asp	Val	Phe	Ile	Ile	Asp	Asp	Ala	Asp	Glu	Ile	Pro	Ala	Arg
			340					345					350		
Asp	Gly	Val	Leu	Phe	Leu	Lys	Leu	Tyr	Asp	Gly	Trp	Thr	Glu	Pro	Phe
		355					360					365			
Ala	Phe	His	Met	Arg	Lys	Ser	Leu	Tyr	Gly	Phe	Phe	Trp	Lys	Gln	Pro
	370					375					380				
Gly	Thr	Leu	Glu	Val	Val	Ser	Gly	Cys	Thr	Ile	Asp	Met	Leu	Gln	Ala
385					390					395					400

Val Tyr Gly Leu Asp Gly Ile Arg Leu Arg Arg Arg Gln Tyr Tyr Thr  
405 410 415

Met Pro Asn Phe Arg Gln Tyr Glu Asn Arg Thr Gly His Ile Leu Val  
420 425 430

Gln Trp Ser Leu Gly Ser Pro Leu His Phe Ala Gly Trp His Cys Ser  
435 440 445

Trp Cys Phe Thr Pro Glu Gly Ile Tyr Phe Lys Leu Val Ser Ala Gln  
450 455 460

Asn Gly Asp Phe Pro Arg Trp Gly Asp Tyr Glu Asp Lys Arg Asp Leu  
465 470 475 480

Asn Tyr Ile Arg Ser Leu Ile Arg Thr Gly Gly Trp Phe Asp Gly Thr  
485 490 495

Gln Gln Glu Tyr Pro Pro Ala Asp Pro Ser Glu His Met Tyr Ala Pro  
500 505 510

Lys Tyr Leu Leu Lys Asn Tyr Asp Gln Phe Arg Tyr Leu Leu Glu Asn  
515 520 525

Pro Tyr Arg Glu Pro Lys Ser Thr Val Glu Gly Gly Arg Arg Asn Gln  
530 535 540

Gly Ser Asp Gly Arg Ser Ser Ala Val Arg Gly Lys Leu Asp Thr Thr  
545 550 555 560

Glu Gly Pro Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu  
565 570

<210> 16  
<211> 398  
<212> PRT  
<213> Unknown

<220>  
<223> GalT amino acid sequence from pBlueGalT

<400> 16

Met Arg Leu Arg Glu Pro Leu Leu Ser Gly Ser Ala Ala Met Pro Gly  
1 5 10 15

Ala Ser Leu Gln Arg Ala Cys Arg Leu Leu Val Ala Val Cys Ala Leu  
20 25 30

His	Leu	Gly	Val	Thr	Leu	Val	Tyr	Tyr	Leu	Ala	Gly	Arg	Asp	Leu	Ser	35	40	45	
Arg	Leu	Pro	Gln	Leu	Val	Gly	Val	Ser	Thr	Pro	Leu	Gln	Gly	Gly	Ser	50	55	60	
Asn	Ser	Ala	Ala	Ala	Ile	Gly	Gln	Ser	Ser	Gly	Glu	Leu	Arg	Thr	Gly	65	70	75	80
Gly	Ala	Arg	Pro	Pro	Pro	Pro	Leu	Gly	Ala	Ser	Ser	Gln	Pro	Arg	Pro	85	90	95	
Gly	Gly	Asp	Ser	Ser	Pro	Val	Val	Asp	Ser	Gly	Pro	Gly	Pro	Ala	Ser	100	105	110	
Asn	Leu	Thr	Ser	Val	Pro	Val	Pro	His	Thr	Thr	Ala	Leu	Ser	Leu	Pro	115	120	125	
Ala	Cys	Pro	Glu	Glu	Ser	Pro	Leu	Leu	Val	Gly	Pro	Met	Leu	Ile	Glu	130	135	140	
Phe	Asn	Met	Pro	Val	Asp	Leu	Glu	Leu	Val	Ala	Lys	Gln	Asn	Pro	Asn	145	150	155	160
Val	Lys	Met	Gly	Gly	Arg	Tyr	Ala	Pro	Arg	Asp	Cys	Val	Ser	Pro	His	165	170	175	
Lys	Val	Ala	Ile	Ile	Ile	Pro	Phe	Arg	Asn	Arg	Gln	Glu	His	Leu	Lys	180	185	190	
Tyr	Trp	Leu	Tyr	Tyr	Leu	His	Pro	Val	Leu	Gln	Arg	Gln	Gln	Leu	Asp	195	200	205	
Tyr	Gly	Ile	Tyr	Val	Ile	Asn	Gln	Ala	Gly	Asp	Thr	Ile	Phe	Asn	Arg	210	215	220	
Ala	Lys	Leu	Leu	Asn	Val	Gly	Phe	Gln	Glu	Ala	Leu	Lys	Asp	Tyr	Asp	225	230	235	240
Tyr	Thr	Cys	Phe	Val	Phe	Ser	Asp	Val	Asp	Leu	Ile	Pro	Met	Asn	Asp	245	250	255	
His	Asn	Ala	Tyr	Arg	Cys	Phe	Ser	Gln	Pro	Arg	His	Ile	Ser	Val	Ala	260	265	270	
Met	Asp	Lys	Phe	Gly	Phe	Ser	Leu	Pro	Tyr	Val	Gln	Tyr	Phe	Gly	Gly	275	280	285	

Val Ser Ala Leu Ser Lys Gln Gln Phe Leu Thr Ile Asn Gly Phe Pro  
290 295 300

Asn Asn Tyr Trp Gly Trp Gly Gly Glu Asp Asp Asp Ile Phe Asn Arg  
305 310 315 320

Leu Val Phe Arg Gly Met Ser Ile Ser Arg Pro Asn Ala Val Val Gly  
325 330 335

Arg Cys Arg Met Ile Arg His Ser Arg Asp Lys Lys Asn Glu Pro Asn  
340 345 350

Pro Gln Arg Phe Asp Arg Ile Ala His Thr Lys Glu Thr Met Leu Ser  
355 360 365

Asp Gly Leu Asn Ser Leu Thr Tyr Gln Val Leu Asp Val Gln Arg Tyr  
370 375 380

Pro Leu Tyr Thr Gln Ile Thr Val Asp Ile Gly Thr Pro Ser  
385 390 395

<210> 17  
<211> 3435  
<212> DNA  
<213> Homo sapiens

<400> 17  
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ggctccttcc ctcagggcca gctctcaatg ttgcaagaaa aaatagacca tttggagcgt 180  
ttgctagctg agaataatga gatcatctca aatattagag actcagtcac caatttgagt 240  
gagtctgtgg aggatggtcc gaaaagttca caaagcaatt tcagccaagg tgctggctca 300  
catcttctgc cctcacaatt atccctctca gttgacactg cagactgtct gtttgcttca 360  
caaagtggaa gtcacaattc agatgtgcag atgttggtatg ttacagtcct aatttctttt 420  
gacaatccag atggtggagt ttggaagcaa ggatttgaca ttacttatga atctaataa 480  
tgggacactg aacccttca agtctttgtg gtgcctcatt ccataacga ccaggttg 540  
ttgaagactt tcaatgacta ctttagagac aagactcagt atatttttaa taacatggtc 600  
ctaaagctga aagaagactc acggaggaag tttatttggt ctgagatctc ttacctttca 660  
aagtgggtgg atattataga tattcagaag aaggatgctg ttaaaagttt aatagaaaat 720  
ggtcagcttg aaattgtgac aggtggctgg gttatgcctg atgaagctac tccacattat 780  
tttgccttaa ttgatcaact aattgaagga catcagtggc tggaaaataa tataggagt 840

aaacctcggg	cgggctgggc	tattgatccc	tttggacact	caccaacaat	ggcttatctt	900
ctaaaccgtg	ctggactttc	tcacatgctt	atccagagag	ttcattatgc	agttaaaaaa	960
cactttgcac	tgcataaaac	attggagttt	ttttggagac	agaattggga	tctgggatct	1020
gtcacagata	ttttatgcca	catgatgccc	ttctacagct	atgacatccc	tcacacttgt	1080
ggacctgatc	ctaaaatatg	ctgccagttt	gatttttaaac	gtcttcctgg	aggcagattt	1140
ggttgtccct	ggggagtccc	cccagaaaca	atacatcctg	gaaatgtcca	aagcagggct	1200
cggatgctac	tagatcagta	cggaaagaag	tcaaagcttt	ttcgtaccaa	agttctcctg	1260
gctccactag	gagatgattt	ccgctactgt	gaatacacgg	aatgggattt	acagtttaag	1320
aattatcagc	agctttttga	ttatatgaat	tctcagtcca	agtttaaagt	taagatacag	1380
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gatcattact	ggagtggcta	ttttacatcc	agaccctttt	acaaacgaat	ggacagaatc	1560
atggaatctc	atttaagggc	tgctgaaatt	ctttactatt	tcgccctgag	acaagctcac	1620
aaatacaaga	taaataaatt	tctctcatca	tcactttaca	cggcactgac	agaagccaga	1680
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gcctatgaga	tctcttttcg	agcacatata	ccgccattgg	gactgaaagt	gtataagatt	2160
ttggaatcag	caagttcaaa	ttcacattta	gctgattatg	tcttgtataa	gaataaagta	2220
gaagatagcg	gaattttcac	cataaagaat	atgataaata	ctgaagaagg	tataacacta	2280
gagaactcct	ttgttttact	tcggtttgat	caaactggac	ttatgaagca	aatgatgact	2340
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Val Val Ile Phe Ser Leu Tyr Leu Met Leu Asp Arg Gly His Leu Asp
20 25 30

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Tyr Pro Arg Asn Pro Arg Arg Glu Gly Ser Phe Pro Gln Gly Gln Leu
35 40 45

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Ser Met Leu Gln Glu Lys Ile Asp His Leu Glu Arg Leu Leu Ala Glu
50 55 60

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Asn Asn Glu Ile Ile Ser Asn Ile Arg Asp Ser Val Ile Asn Leu Ser
65 70 75 80

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Glu Ser Val Glu Asp Gly Pro Lys Ser Ser Gln Ser Asn Phe Ser Gln
85 90 95

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Gly Ala Gly Ser His Leu Leu Pro Ser Gln Leu Ser Leu Ser Val Asp
100 105 110

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Thr Ala Asp Cys Leu Phe Ala Ser Gln Ser Gly Ser His Asn Ser Asp  
115 120 125

Val Gln Met Leu Asp Val Tyr Ser Leu Ile Ser Phe Asp Asn Pro Asp  
130 135 140

Gly Gly Val Trp Lys Gln Gly Phe Asp Ile Thr Tyr Glu Ser Asn Glu  
145 150 155 160

Trp Asp Thr Glu Pro Leu Gln Val Phe Val Val Pro His Ser His Asn  
165 170 175

Asp Pro Gly Trp Leu Lys Thr Phe Asn Asp Tyr Phe Arg Asp Lys Thr  
180 185 190

Gln Tyr Ile Phe Asn Asn Met Val Leu Lys Leu Lys Glu Asp Ser Arg  
195 200 205

Arg Lys Phe Ile Trp Ser Glu Ile Ser Tyr Leu Ser Lys Trp Trp Asp  
210 215 220

Ile Ile Asp Ile Gln Lys Lys Asp Ala Val Lys Ser Leu Ile Glu Asn  
225 230 235 240

Gly Gln Leu Glu Ile Val Thr Gly Gly Trp Val Met Pro Asp Glu Ala  
245 250 255

Thr Pro His Tyr Phe Ala Leu Ile Asp Gln Leu Ile Glu Gly His Gln  
260 265 270

Trp Leu Glu Asn Asn Ile Gly Val Lys Pro Arg Ser Gly Trp Ala Ile  
275 280 285

Asp Pro Phe Gly His Ser Pro Thr Met Ala Tyr Leu Leu Asn Arg Ala  
290 295 300

Gly Leu Ser His Met Leu Ile Gln Arg Val His Tyr Ala Val Lys Lys  
305 310 315 320

His Phe Ala Leu His Lys Thr Leu Glu Phe Phe Trp Arg Gln Asn Trp  
325 330 335

Asp Leu Gly Ser Val Thr Asp Ile Leu Cys His Met Met Pro Phe Tyr  
340 345 350

Ser Tyr Asp Ile Pro His Thr Cys Gly Pro Asp Pro Lys Ile Cys Cys

355 360 365

Gln Phe Asp Phe Lys Arg Leu Pro Gly Gly Arg Phe Gly Cys Pro Trp  
370 375 380

Gly Val Pro Pro Glu Thr Ile His Pro Gly Asn Val Gln Ser Arg Ala  
385 390 395 400

Arg Met Leu Leu Asp Gln Tyr Arg Lys Lys Ser Lys Leu Phe Arg Thr  
405 410 415

Lys Val Leu Leu Ala Pro Leu Gly Asp Asp Phe Arg Tyr Cys Glu Tyr  
420 425 430

Thr Glu Trp Asp Leu Gln Phe Lys Asn Tyr Gln Gln Leu Phe Asp Tyr  
435 440 445

Met Asn Ser Gln Ser Lys Phe Lys Val Lys Ile Gln Phe Gly Thr Leu  
450 455 460

Ser Asp Phe Phe Asp Ala Leu Asp Lys Ala Asp Glu Thr Gln Arg Asp  
465 470 475 480

Lys Gly Gln Ser Met Phe Pro Val Leu Ser Gly Asp Phe Phe Thr Tyr  
485 490 495

Ala Asp Arg Asp Asp His Tyr Trp Ser Gly Tyr Phe Thr Ser Arg Pro  
500 505 510

Phe Tyr Lys Arg Met Asp Arg Ile Met Glu Ser His Leu Arg Ala Ala  
515 520 525

Glu Ile Leu Tyr Tyr Phe Ala Leu Arg Gln Ala His Lys Tyr Lys Ile  
530 535 540

Asn Lys Phe Leu Ser Ser Ser Leu Tyr Thr Ala Leu Thr Glu Ala Arg  
545 550 555 560

Arg Asn Leu Gly Leu Phe Gln His His Asp Ala Ile Thr Gly Thr Ala  
565 570 575

Lys Asp Trp Val Val Val Asp Tyr Gly Thr Arg Leu Phe His Ser Leu  
580 585 590

Met Val Leu Glu Lys Ile Ile Gly Asn Ser Ala Phe Leu Leu Ile Leu  
595 600 605



Lys Asp Lys Leu Thr Tyr Asp Ser Tyr Ser Pro Asp Thr Phe Leu Glu  
 610 615 620  
 Met Asp Leu Lys Gln Lys Ser Gln Asp Ser Leu Pro Gln Lys Asn Ile  
 625 630 635 640  
 Ile Arg Leu Ser Ala Glu Pro Arg Tyr Leu Val Val Tyr Asn Pro Leu  
 645 650 655  
 Glu Gln Asp Arg Ile Ser Leu Val Ser Val Tyr Val Ser Ser Pro Thr  
 660 665 670  
 Val Gln Val Phe Ser Ala Ser Gly Lys Pro Val Glu Val Gln Val Ser  
 675 680 685  
 Ala Val Trp Asp Thr Ala Asn Thr Ile Ser Glu Thr Ala Tyr Glu Ile  
 690 695 700  
 Ser Phe Arg Ala His Ile Pro Pro Leu Gly Leu Lys Val Tyr Lys Ile  
 705 710 715 720  
 Leu Glu Ser Ala Ser Ser Asn Ser His Leu Ala Asp Tyr Val Leu Tyr  
 725 730 735  
 Lys Asn Lys Val Glu Asp Ser Gly Ile Phe Thr Ile Lys Asn Met Ile  
 740 745 750  
 Asn Thr Glu Glu Gly Ile Thr Leu Glu Asn Ser Phe Val Leu Leu Arg  
 755 760 765  
 Phe Asp Gln Thr Gly Leu Met Lys Gln Met Met Thr Lys Glu Asp Gly  
 770 775 780  
 Lys His His Glu Val Asn Val Gln Phe Ser Trp Tyr Gly Thr Thr Ile  
 785 790 795 800  
 Lys Arg Asp Lys Ser Gly Ala Tyr Leu Phe Leu Pro Asp Gly Asn Ala  
 805 810 815  
 Lys Pro Tyr Val Tyr Thr Thr Pro Pro Phe Val Arg Val Thr His Gly  
 820 825 830  
 Arg Ile Tyr Ser Glu Val Thr Cys Phe Phe Asp His Val Thr His Arg  
 835 840 845  
 Val Arg Leu Tyr His Ile Gln Gly Ile Glu Gly Gln Ser Val Glu Val

850		855		860
Ser Asn Ile Val Asp	Ile Arg Lys Val Tyr	Asn Arg Glu Ile Ala Met		
865	870	875		880
Lys Ile Ser Ser Asp	Ile Lys Ser Gln Asn Arg Phe Tyr Thr	Asp Leu		
	885	890		895
Asn Gly Tyr Gln Ile Gln Pro Arg Met Thr Leu Ser Lys Leu Pro Leu				
	900	905		910
Gln Ala Asn Val Tyr Pro Met Thr Thr Met Ala Tyr Ile Gln Asp Ala				
	915	920		925
Lys His Arg Leu Thr Leu Leu Ser Ala Gln Ser Leu Gly Val Ser Ser				
	930	935		940
Leu Asn Ser Gly Gln Ile Glu Val Ile Met Asp Arg Arg Leu Met Gln				
	945	950		955
Asp Asp Asn Arg Gly Leu Glu Gln Gly Ile Gln Asp Asn Lys Ile Thr				
	965	970		975
Ala Asn Leu Phe Arg Ile Leu Leu Glu Lys Arg Ser Ala Val Asn Thr				
	980	985		990
Glu Glu Glu Lys Lys Ser Val Ser Tyr Pro Ser Leu Leu Ser His Ile				
	995	1000		1005
Thr Ser Ser Leu Met Asn His Pro Val Ile Pro Met Ala Asn Lys				
	1010	1015		1020
Phe Phe Ser Pro Thr Leu Glu Leu Gln Gly Glu Phe Ser Pro Leu				
	1025	1030		1035
Gln Ser Ser Leu Pro Cys Asp Ile His Leu Val Asn Leu Arg Thr				
	1040	1045		1050
Ile Gln Ser Lys Val Gly Asn Gly His Ser Asn Glu Ala Ala Leu				
	1055	1060		1065
Ile Leu His Arg Lys Gly Phe Asp Cys Arg Phe Ser Ser Lys Gly				
	1070	1075		1080
Thr Gly Leu Phe Cys Ser Thr Thr Gln Gly Lys Ile Leu Val Gln				
	1085	1090		1095

Lys Leu Leu Asn Lys Phe Ile Val Glu Ser Leu Thr Pro Ser Ser  
1100 1105 1110

Leu Ser Leu Met His Ser Pro Pro Gly Thr Gln Asn Ile Ser Glu  
1115 1120 1125

Ile Asn Leu Ser Pro Met Glu Ile Ser Thr Phe Arg Ile Gln Leu  
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<212> DNA  
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ggctccttcc ctcagggcca gctctcaatg ttgcaagaaa aaatagacca tttggagcgt 180  
ttgctagctg agaataatga gatcatctca aatattagag actcagtcac caatttgagt 240  
gagtctgtgg aggatggtcc gaaaagttca caaagcaatt tcagccaagg tgctggctca 300  
cccgctgcc ctgaggagtc ccgctgctt gtgggccccca tgctgattga gtttaacatg 360  
cctgtggacc tggagctcgt ggcaaagcag aacccaaatg tgaagatggg cgcccgctat 420  
gccccaggg actgcgtctc tctcacaag gtggccatca tcattccatt ccgcaaccgg 480  
caggagcacc tcaagtactg gctatatatt ttgcaccag tctgcagcg ccagcagctg 540  
gactatggca tctatgttat caaccaggcg ggagacacta tattcaatcg tgctaagctc 600  
ctcaatgttg gctttcaaga agccttgaag gactatgact acacctgctt tgtgtttagt 660  
gacgtggacc tcattccaat gaatgaccat aatgcgtaca ggtgtttttc acagccacgg 720  
cacatttccg ttgcaatgga taagtgttga ttcagcctac cttatgttca gtatttttga 780  
ggtgtctctg ctctaagtaa acaacagttt ctaaccatca atggatttcc taataattat 840  
tggggctggg gaggagaaga tgatgacatt tttaacagat tagtttttag aggcattgtct 900  
atatctcgcc caaatgctgt ggtcgggagg tgtcgcatga tccgccactc aagagacaaa 960  
aaaaatgaac ccaatcctca gaggtttgac cgaattgcac acacaaagga gacaatgctc 1020  
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<220>  
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Val Val Ile Phe Ser Leu Tyr Leu Met Leu Asp Arg Gly His Leu Asp  
20 25 30

Tyr Pro Arg Asn Pro Arg Arg Glu Gly Ser Phe Pro Gln Gly Gln Leu  
35 40 45

Ser Met Leu Gln Glu Lys Ile Asp His Leu Glu Arg Leu Leu Ala Glu  
50 55 60

Asn Asn Glu Ile Ile Ser Asn Ile Arg Asp Ser Val Ile Asn Leu Ser  
65 70 75 80

Glu Ser Val Glu Asp Gly Pro Lys Ser Ser Gln Ser Asn Phe Ser Gln  
85 90 95

Gly Ala Gly Ser Pro Ala Cys Pro Glu Glu Ser Pro Leu Leu Val Gly  
100 105 110

Pro Met Leu Ile Glu Phe Asn Met Pro Val Asp Leu Glu Leu Val Ala  
115 120 125

Lys Gln Asn Pro Asn Val Lys Met Gly Gly Arg Tyr Ala Pro Arg Asp  
130 135 140

Cys Val Ser Pro His Lys Val Ala Ile Ile Ile Pro Phe Arg Asn Arg  
145 150 155 160

Gln Glu His Leu Lys Tyr Trp Leu Tyr Tyr Leu His Pro Val Leu Gln  
165 170 175

Arg Gln Gln Leu Asp Tyr Gly Ile Tyr Val Ile Asn Gln Ala Gly Asp  
180 185 190

Thr Ile Phe Asn Arg Ala Lys Leu Leu Asn Val Gly Phe Gln Glu Ala  
195 200 205

Leu Lys Asp Tyr Asp Tyr Thr Cys Phe Val Phe Ser Asp Val Asp Leu  
210 215 220

Ile Pro Met Asn Asp His Asn Ala Tyr Arg Cys Phe Ser Gln Pro Arg  
225 230 235 240

His Ile Ser Val Ala Met Asp Lys Phe Gly Phe Ser Leu Pro Tyr Val  
245 250 255

Gln Tyr Phe Gly Gly Val Ser Ala Leu Ser Lys Gln Gln Phe Leu Thr  
260 265 270

Ile Asn Gly Phe Pro Asn Asn Tyr Trp Gly Trp Gly Gly Glu Asp Asp  
275 280 285

Asp Ile Phe Asn Arg Leu Val Phe Arg Gly Met Ser Ile Ser Arg Pro  
290 295 300

Asn Ala Val Val Gly Arg Cys Arg Met Ile Arg His Ser Arg Asp Lys  
305 310 315 320

Lys Asn Glu Pro Asn Pro Gln Arg Phe Asp Arg Ile Ala His Thr Lys  
325 330 335

Glu Thr Met Leu Ser Asp Gly Leu Asn Ser Leu Thr Tyr Gln Val Leu  
340 345 350

Asp Val Gln Arg Tyr Pro Leu Tyr Thr Gln Ile Thr Val Asp Ile Gly  
355 360 365

Thr Pro Ser  
370